CONFIDENTIAL

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AFFINITY™ ANTERIOR CERVICAL CAGE SYSTEM
Important Medical Information

CAUTION: Federal (USA) law restricts this device to sale by or on the order of a physician with appropriate training or experience.

The following contains important medical information on the AFFINITY™ Anterior Cervical Cage System.

DESCRIPTION:

The AFFINITY™ Anterior Cervical Cage System consists of a hollow, threaded, tapered metal device which inserts into the intervertebral disc space. The AFFINITY™ implants are available in diameters ranging from 6 mm to 12 mm and in lengths ranging from 12 mm to 14 mm.

The AFFINITY™ implants are made from implant grade titanium alloy (Ti-6Al-4V) described by ASTM F136 or its ISO equivalent.

No warranties, expressed or implied, are made. Implied warranties of merchantability and fitness for a particular use are specifically excluded.

INDICATIONS:

The AFFINITY™ Anterior Cervical Cage System is indicated for anterior cervical interbody fusion procedures in skeletally mature patients with cervical disc disease at one level from the C2-C3 disc to the C7-T1 disc. Cervical disc disease is defined as intractable radiculopathy and/or myelopathy with herniated disc and/or osteophyte formation on posterior vertebral endplates producing symptomatic nerve root and/or spinal cord compression confirmed by radiographic studies. AFFINITY™ implants are to be used with autogenous bone graft and implanted via an open, anterior approach.

CONTRAINDICATIONS:

The AFFINITY™ Anterior Cervical Cage System should not be implanted in patients with an active infection or with an allergy to titanium or titanium alloy.

PRECAUTIONS:

- CAUTION: The AFFINITY™ Anterior Cervical Cage System should only be used by surgeons who are experienced in cervical interbody fusion procedures and have undergone adequate training with this device. A lack of adequate experience and/or training may lead to a higher incidence of adverse events, such as neurological complications.

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ADVERSE EVENTS:

The adverse events, as shown in Table 1, were reported from the 202 AFFINITY™ device patients and 62 control patients enrolled in multi-center clinical studies. The control treatment was a single level anterior interbody fusion procedure with iliac crest-derived autogenous bone.

The following table lists the adverse events in alphabetical order. Note: Some patients experienced more than one adverse event.

TABLE I - ADVERSE EVENTS

Adverse Event	Surgery		Postoperative (1 day to 1 Month)		6 Weeks (1 Month to 2 Months)		3 Months (2 Months to 5 Months)		6 Months (5 Months to 9 Months)		12 Months (9 Months to 19 Months)		24 Months (or greater) (19 Months to 48 Months)		Total Adverse Events	
	AFFINITY N=202	Control[1] N=62	AFFINITY N=202	Control N=62	AFFINITY N=200	Control N=58	AFFINITY N=191	Control N=58	AFFINITY N=186	Control N=57	AFFINITY N=178	Control N=50	AFFINITY N=174	Control N=47	AFFINITY	Control
Anatomical/ Technical Difficulty	1	3	0	0	0	0	0	0	0	0	0	0	0	0	1	3
Cancer	0	0	0	0	0	0	0	0	1	0	1	0	0	0	2	0
Cardio/Vascular	0	0	3	2	0	0	0	0	0	0	1	3	1	1	5	6
Carpal Tunnel Syndrome	0	0	0	0	0	0	1	0	1	0	5	0	0	0	7	0
Dural Tear	1	0	0	0	0	0	0	0	0	0	0	0	0	0	1	0
Dysphonia/Dysphagia	0	0	5	4	3	0	0	2	0	0	0	0	0	0	8	6
Gastrointestinal	0	0	7	0	1	1	0	0	0	0	5	1	3	0	16	2
Graft Site Related	0	0	5	2	0	1	0	0	0	0	0	0	0	0	5	3
Implant Displacement/ Loosening Collapse	0	0	0	1	0	2	0	3	0	2	0	1	0	0	0	9
Infection	0	0	5	0	1	0	0	0	0	1	1	2	0	2	7	5
Malpositioned Implant	0	0	1	0	0	0	0	0	0	0	0	0	0	0	1	0
Neck and/or Arm Pain	0	0	2	0	7	0	5	2	5	1	10	2	6	1	35	6
Neurological																
Upper Body[2]	0	0	1	4	3	1	1	3	0	3	5	2	3	4	13	17
Lower Body[3]	0	0	0	1	1	0	0	1	0	1	0	2	1	0	2	5
Non-Union[4]	0	0	0	0	0	0	0	0	3	2	2	1	3	2	8	5
Non-Union Pending[5]	0	0	0	0	0	0	1	3	1	0	1	2	1	0	4	5
Other Pain[6]	0	0	1	0	1	0	1	1	2	0	5	1	3	2	13	4
Respiratory	0	1	0	1	0	0	0	0	0	0	0	0	0	0	0	2
Spinal Event:																
Cervical Spine	0	0	0	0	2	0	3	3	2	0	5	3	3	2	15	8
Thoracic Spine	0	0	0	0	0	0	1	0	0	0	0	0	0	0	1	0
Lumbar Spine	0	0	0	0	0	0	5	0	5	1	2	0	1	0	13	1
Subsidence	0	0	0	0	0	0	1	0	0	0	0	0	0	0	1	0
Trauma	0	0	3	0	1	0	10	1	6	1	5	0	5	4	30	6
Urogenital	0	0	2	4	0	0	0	0	2	0	0	1	1	0	5	5
Vascular Intra-op	0	1	0	0	0	0	0	0	0	0	0	0	0	0	0	1
Other[7]	0	0	3	2	1	0	0	1	0	1	6	1	6	4	16	9

[1] Control = Patients receiving the autograft treatment.

[2] Neurological adverse events that affected the upper body, i.e., arms, neck, etc.

[3] Neurological adverse events that affected the lower body, i.e, legs, feet, etc.

[4] Non-union adverse events that have resulted in a second surgery.

[5] Non-union adverse events that have not resulted in a second surgery.

[6] "Other pain" consists of pain that is not related to the surgery or the treatment area. Examples are bursitis, knee pain, back pain, migraine headaches.

[7] The "Other" adverse event category consists of the following adverse events reported in the clinical trial: allergy/rash, allergic reaction to chemotherapy, chemotherapy side effects, cholecystectomy, diabetes, elevated temperature, fibromyalgia, hardware removal, hearing loss and cataracts, hepatomegaly, Horner's Syndrome, joint crepitus, low B12 and folate, malpositioned cervical plate, narcotic addiction, psychological disorder, and toothache.

The most noteworthy adverse events in the AFFINITY™ device group were neurological complications and spinal events. A total of 15 upper and lower body neurological events occurred in 15 patients in the AFFINITY™ device group. These events included: 9 events of tingling and/or numbness in arms or hands either with or without associated pain; 2 cases of new myelopathy; 1 event producing leg numbness symptoms; 1 case of hand cramping; 1 Morton's neuroma of the foot; and 1 median nerve entrapment which was not carpal tunnel.

A total of 29 spinal events occurred in 27 patients in the AFFINITY™ device group. These events included the following: 6 cervical spondyloses, 4 cases of herniated nucleus pulposus in the cervical spine; 3 cervical degenerative disc disease; 1 cervical arthritis; 1 bone spur; 1 thoracic herniated nucleus pulposus and 13 lumbar associated events, such as degenerative disc disease.

In addition, there were 29 patients in the AFFINITY™ device group who had 35 reports of neck and/or arm pain. Of the 14 events reported between surgery discharge and 6 months postoperatively, 7 involved neck pain including muscle cramps or strains, 6 involved shoulder or arm pain including rotator cuff injuries, and 1 involved hand pain. Of the 10 events occurring between 6 and 12 months postoperatively, 5 involved neck and arm pain, 4 involved shoulder pain including 1 rotator cuff tendonitis, and 1 involved cervical muscle pain and headache. Eleven events occurred at least 12 months after the initial surgery. Of these, 3 involved shoulder pain, 4 involved neck and/or arm pain, 1 involved arm pain associated with fatigue, 1 involved joint pain in neck, shoulders, back, and hands, 1 involved elbow pain, and 1 involved thoracic pain.

In addition to the 35 reports of neck/arm pain, Table 1 includes 15 patients who reported hand pain. Of the 50 patients reporting neck/arm/hand pain symptoms, 35 of the complaints could be attributed to the operative or adjacent levels. Of the 50 patients complaining of postoperative neck, arm and hand symptoms, 10 were considered neck pain failures and 7 were considered arm pain failures according to the success/failure criteria.

Table II presents the Bayesian statistical comparison of adverse events between the AFFINITY™ device group and the control treatment group.

Table II - Bayesian Comparison of Adverse Events		
Adverse Event	**There is a 95% Probability that adverse event rates will fall between the following ranges**	
	AFFINITY ™ Device	**Control**
Anatomical/Technical Difficulty	0% to 3%	2% to 13%
Cancer	0% to 4%	0% to 6%
Cardio/Vascular	2% to 32%	6% to 52%
Carpal Tunnel	2% to 7%	0% to 6%
Dural Tear	0% to 3%	0% to 6%
Dysphonia/Dysphagia	3% to 11%	2% to 15%
Gastrointestinal	6% to 15%	1% to 9%
Graft Site Related	2% to 47%	3% to 54%
Implant Collapse/ Displacement/Loosening	0% to 2%	8% to 25%
Infection	2% to 10%	0% to 12%
Malpositioned Implant	0% to 3%	0% to 6%
Neck and/or Arm Pain	12% to 23%	3% to 16%
Neurological	4% to 12%	26% to 53%
Non-Union (Outcome Pending)	1% to 7%	2% to 21%
Other Pain	3% to 11%	2% to 19%
Respiratory	0% to 2%	1% to 11%
Spinal Event	10% to 23%	7% to 27%
Subsidence	0% to 3%	0% to 6%
Trauma	5% to 47%	6% to 35%
Urogenital	1% to 7%	3% to 23%
Vascular Intraop	0% to 2%	0% to 9%
Other Adverse Event	5% to 13%	5% to 24%
Any Adverse Event	46% to 60%	55% to 81%

Some of the adverse events led to surgical interventions subsequent to the clinical trial surgery. These surgical interventions can be classified as revisions, removals, supplemental fixations, reoperations, and other (see footnotes below Table III for an explanation of these terms). Table III summarizes the secondary surgical interventions in the AFFINITY™ device and control treatment groups in the 12-Month and 24-Month post-operative intervals. Table III also presents the Bayesian statistical comparison of secondary surgeries between the AFFINITY™ device group and the control treatment group.

Table III - Secondary Surgical Procedures								
Clinical Comparison of Secondary Surgeries							Bayesian Statistical Comparison of Second Surgeries	
Type of Secondary Surgical Procedure	Up to 12 Months (1 day to 19 Months)		24 Months or Later (19 Months to 48 Months)		Total Events[4]		There is a 95% Probability that Second Surgery rates will fall between the following ranges	
Type of Secondary Surgical Procedure[3]	AFFINITY™ N=178	Control[1] N=50	AFFINITY™ N=174	Control N=47	AFFINITY™	Control	AFFINITY™ Cage System	Control
Revision	3	5	0	2	3	7	1% to 31%	6% to 58%
Removal	2	0	3	0	5	0	1% to 6%	0% to 6%
Supplemental Fixation	5	0	1	0	6	0	1% to 6%	0% to 6%
Reoperation	1	2	1	0	2	2	0% to 4%	1% to 11%
Other[2]	27	5	4	3	31	8	9% to 19%	8% to 30%

[1] Control, i.e., patients receiving the autograft treatment

[2] Other Second Surgery is any surgical procedure not classified as a revision, removal, supplemental fixation, or a reoperation such as surgeries for hernias, rotator cuff tears, lumbar adverse events, carpal tunnel syndrome, cervical adverse events that occurred at a different level, etc.

[3] **Revision:** A procedure that adjusts or in any way modifies the original implant configuration.
Removal: A procedure at the involved level that removes one or more components of the original implant configuration without replacement with the same type of trial device.
Supplemental Fixation: A procedure at the involved level in which additional cervical fixation devices that are not approved as part of the protocol are placed.
Reoperation: Any surgical procedure at the involved level that is not classified as a Removal, Revision, or Supplemental Fixation, such as a procedure for wound drainage of the graft site.
Other: Any surgical procedure not classified as a revision, removal, supplemental fixation, or a reoperation, such as surgeries for hernias, rotator cuff tears, lumbar adverse events, carpal tunnel syndrome, cervical adverse events that occurred at a different level, etc.

[4] Some patients experienced more than one second surgery.

Of the 47 patients in the AFFINITY™ device group who required a second surgery, 8 had surgery for non-union, 7 had surgery for neck and/or arm pain, 5 had surgery to treat a lumbar condition, 5 required surgery due to trauma, and 3 had surgery to treat carpal tunnel syndrome. Most of the second surgeries occurred up to and including the 12-Month post-operative interval.

Potential Adverse Events:

The following is a list of potential adverse events which may occur with cervical interbody fusion surgery with the AFFINITY™ Anterior Cervical Cage System. Some of these adverse events may have been previously reported in the adverse events table.

- Bending, breakage, loosening, and/or migration of components
- Foreign body (allergic) reaction
- Tissue or nerve damage
- Post-operative change in spinal curvature, loss of correction, height, and/or reduction
- Infection
- Dural tears
- Neurological system compromise
- Dysphagia/dysphonia
- Scar formation
- Bone fracture
- Non-union (or pseudarthrosis), delayed union, mal-union
- Cessation of any potential growth of the operated portion of the spine. Loss of spinal mobility or function
- Graft donor site complications
- Damage to blood vessels and cardiovascular system compromise
- Gastrointestinal complications
- Damage to internal organs and connective tissue
- Development of respiratory problems
- Incisional complications
- Change in mental status
- Death

Note: Additional surgery may be necessary to correct some of these potential adverse events.

CLINICAL RESULTS:

Study Design and Purpose

A prospective, multi-center, controlled clinical trial of the AFFINITY™ Anterior Cervical Cage System was conducted in the United States to determine the safety and effectiveness of the anterior cervical use of the AFFINITY™ device in the treatment of patients with symptomatic cervical disc disease. Investigational patients were treated with the AFFINITY™ device filled with autogenous bone derived from the iliac crest. Control patients were treated with iliac crest-derived autogenous bone.

The effectiveness measures selected for this investigation included whether the treated disc level fused, whether there was relief from neck pain and disability, and whether the neurologic status was maintained or improved. Safety was evaluated with an analysis of reported adverse events and second surgeries.

Methods

Inclusion criteria for the clinical trial included symptomatic cervical disc disease as noted by intractable radiculopathy and/or myelopathy with herniated disc and/or osteophyte formation on posterior vertebral endplates producing symptomatic nerve root and/or spinal cord compression documented by diagnostic imaging finding(s); single level involvement from C2-C3 disc to C7-T1 disc; unresponsive to 6 weeks conservative treatment or the presence of progressive symptoms or signs of nerve root or spinal cord compression in the face of continued non-operative management. Specifically excluded from the clinical trial were patients who had: a previous surgical intervention at the involved spinal level; osteopenia, osteoporosis, or osteomalacia or metabolic bone disease; instability greater than 3.5 mm translation or 11° of angular motion; overt or active spinal and/or systemic infection; pregnancy ; or a condition which required postoperative medications that interfere with fusion such as steroids.

Patients were evaluated preoperatively, perioperatively, and postoperatively at 6 weeks, 3, 6, 12, and 24 months. For this clinical trial, overall success was the primary endpoint. Overall success was based on a patient demonstrating fusion, pain and disability success, neurological success, and no secondary surgical procedure classified as a revision, removal or supplemental fixation. Fusion was based on angular motion and lucent line criteria and was assessed from static and dynamic radiographs. Pain and disability were measured using the Neck Disability Index. Success was based on the postoperative score being better than the preoperative score by at least 15 points if the preoperative score was at least 30 points or by at least 50% if the preoperative score was less than 30 points. If the preoperative NDI score was zero, the postoperative score also had to be zero for success. Neurological status was evaluated based on sensory, motor, reflex, and foraminal compression test assessments and success was based on a postoperative maintenance or improvement in condition as compared to the preoperative status.

Statistical Analyses

The results of the clinical study were evaluated using Bayesian statistical methods. All patients involved in the clinical trial of the AFFINITY™ Anterior Cervical Cage System and the control group studies were enrolled under the same inclusion/exclusion criteria. To substantiate the comparability of the two groups, a logistic regression analysis was performed which examined the relationship of all demographic, preoperative medical conditions and preoperative measurements of effectiveness variables on the overall success results. All preoperative variables were considered as covariate candidates and the five most influential ones (gender, preoperative work status, tobacco use, neurological compression test (F.C.T.) reaction, and whether a patient had preoperative radicular symptoms) were incorporated into covariate analyses of the outcome parameters, thereby adjusting the posterior probabilities in accordance with their influence. Consequently, based on this statistical methodology, the most influential prognostic differences between the two treatment groups for demographic and preoperative information were taken into account in assessing the outcome parameters.

A small fraction of the patients did not have their 24-month postoperative evaluations when the results were analyzed. Their 24-month results were predicted from their 12-month outcomes and the relationship established from patients that had both 12 and 24-month evaluations.

Patient Population

A total of 202 patients were enrolled in the investigational AFFINITY™ device treatment group and a total of 62 control patients were entered into clinical studies in both the U.S. and U.K. The mean ages for patients in the AFFINITY™ device and control treatment groups were 44.5 and 50.1 years, respectively. Approximately 52% of the AFFINITY™ device patients were males as compared to 57% for the control group. Tobacco use in the control group occurred in approximately 48% of the patients and in 36% of the AFFINITY™ device patients. Over 64% of the AFFINITY™ device patients were working prior to surgery as compared to a 31% rate for the control patients.

Results

The adjusted posterior means of success probabilities for the primary effectiveness parameters, including overall success, at 24 months postoperative can be found in Table IV.

Table IV – Posterior Means (95% HPD Credible Intervals) of Success Probabilities for Primary Effectiveness Variables		
	24 Months	
	AFFINITY™ Device Success Rate (Range*)	**Control** Success Rate (Range*)
Overall Success	68% (60% to 74%)	61% (48% to 75%)
Fusion	94% (63% to 97%)	86% (68% to 99%)
NDI Pain/Disability Improvement	75% (68% to 81%)	75% (62% to 87%)
Neurological Status Maintenance or Improvement	96% (87% to 100%)	78% (45% to 92%)

* There is a 95% probability that success rates will fall between the ranges listed.

In Table IV, neurological success is defined as success in 3 of the 4 subsections (sensory, motor, reflex, and foraminal compression test) as per the protocol. If neurological success required successes in 4 of 4 subsections, 13 of 171 AFFINITY™ device patients and 16 of 45 control patients would not be a neurological success. Of the 13 AFFINITY™ patients, there were ten patients with reflex deficits and three with sensory deficits. Eight of these deficits are associated with the operative or adjacent levels.

PACKAGING:

Packages for each of the components should be intact upon receipt. If a loaner or consignment system is used, all sets should be carefully checked for completeness and all components including instruments should be carefully checked to ensure that there is no damage prior to use. Damaged packages or products should not be used, and should be returned to Medtronic Sofamor Danek.

CLEANING AND DECONTAMINATION:

If not supplied sterile, all implants and instruments must first be cleaned using established hospital methods before sterilization and introduction into a sterile surgical field. Used instruments must be decontaminated, cleaned, and sterilized before reuse. Also, some instruments, such as the reamer/T-handle, require dismantling before cleaning.

Cleaning and disinfecting of instruments can be performed with alkali aldehdye-free solvents at higher temperatures. Cleaning and decontamination can include the use of neutral cleaners followed by a deionized water rinse.

Note: Certain cleaning solutions such as those containing formalin, glutaraldehyde, bleach and/or other alkaline cleaners may damage some devices, particularly instruments; these solutions should not be used.

All products should be treated with care. Improper use or handling may lead to damage and possible improper functioning of the device.

STERILIZATION:

If not supplied sterile, the implants and instruments must be sterilized prior to use. Non-sterile implants and instruments are recommended to be steam sterilized by the hospital using one of the following process parameters:

Sterilization Methods			
Method	**Cycle**	**Temperature**	**Exposure Time**
Steam	Gravity	250°F (121°C)	30 Min.
*Steam	Gravity	273°F (134°C)	20 Min.
Steam	Pre-Vacuum	270°F (132°C)	5 Min.

* NOTE: For use of this product and instruments outside the United States, some non-U.S. Health Care Authorities recommend sterilization according to these parameters so as to minimize the potential risk of transmission of Creutzfeldt-Jakob disease, especially of surgical instruments that could come into contact with the central nervous system.

Remove all packaging material prior to sterilization. Only sterile implants and instruments should be used in surgery. No implant should be re-used once it comes into contact with human tissue or body fluid. Always immediately clean and re-sterilize instruments that have been used in surgery. This process must be performed before handling or (if applicable) returning to Medtronic Sofamor Danek.

PRODUCT COMPLAINTS:

Any health care professional (e.g., customer or user of this system of products), who has any complaints or who has experienced any dissatisfaction in the quality, identification, durability, reliability, safety, effectiveness and/or performance of this product, should notify the distributor, Medtronic Sofamor Danek. Further, if any of the implanted AFFINITY™ Anterior Cervical Cage System components ever "malfunction," (i.e., do not meet any of their performance specifications or otherwise do not perform as intended), or are suspected of doing so, the distributor should be notified immediately. If any Medtronic Sofamor Danek product ever "malfunctions" and may have caused or contributed to the death or serious injury of a patient, the distributor should be notified immediately by telephone, fax or written correspondence. When filing a complaint, please provide the component name and number, lot number, your name and address, the nature of the complaint and notification of whether a written report from the distributor is requested.

DEVICE RETRIEVAL EFFORTS:

Should it be necessary to remove an AFFINITY™ Anterior Cervical Cage System, please call Medtronic Sofamor Danek.

IN USA

Manager
Customer Service Division **Telephone:** 800-876-3133
Medtronic Sofamor Danek USA 800-933-2635
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